

treatment and could be implemented where economic limitations are important or patients have to travel long distances. More prospective studies are needed.

EP047/#376

MULTI-OMICS CHARACTERIZATION OF CELLULAR STATE DIVERSITY AND BIDIRECTIONAL TUMOR-STROMA/IMMUNE INTERACTIONS IN CERVICAL SQUAMOUS CELL CARCINOMA

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Introduction Cervical cancer ranks as the fourth leading cause of cancer-related deaths among women, with low response rates to immune-checkpoint blockade (ICB).

Methods Here we conducted a multidimensional analysis encompassing single-cell RNA-seq (scRNA-seq), spatial transcriptomics, and spatial proteomics, combined with genetic and pharmacological perturbations to systematically develop a high-resolution and spatially-resolved map of intra-tumoral expression heterogeneity in cervical squamous cell carcinoma (CSCC).

Results Three context-specific tumor states (Epithelial-cytokeratin (Epi-Krt), epithelial-immune (Epi-imm) and epithelial senescence (Epi-Sen)) that recapitulate squamous differentiation substantially alter the tumor immune microenvironment (TIME). Bidirectional interactions between Epi-Krt malignant epithelial cells and MMP11⁺ CAF form an immune exclusionary microenvironment through TGFβ pathway signaling mediated by FABP5. Epi-Imm malignant epithelial cells and NK/T cells interact bidirectionally through interferon signaling. Notably, preliminary analysis of the NACI clinical trial (NCT04516616) demonstrated neoadjuvant chemotherapy (NACT) induce a state transition to Epi-Imm with the extent of this transition being associated with pathological complete remission (pCR) to subsequent ICB treatment.

Conclusion/Implications These findings provide a comprehensive and nuanced understanding of cellular state diversity and have significant implications for developing novel therapeutic strategies in CSCC and potentially other squamous cancers.

EP048/#911

CD112 PROMOTES THE PROGRESSION OF CERVICAL CANCER THROUGH SLC7A11/GPX-4 PATHWAYS

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Introduction Expression of the immunoglobulin superfamily member CD112 was increased in multiple malignancies. Importantly, its expression was observed in both PD-L1 negative and positive tumors. However, the role of CD112 in tumorigenesis and tumor development in cervical cancer has not been elucidated.

Methods The expression of CD112 in cervical cancer tissues was detected using immunohistochemistry (IHC) and gene

expression profiling. CCK-8, Edu tests, wound healing and migration assays were used to assess the biological effects of CD112 overexpression and knockdown. Furthermore, proteomic analysis revealed the potential mechanism of CD112 in cervical cancer.

Results CD112 is expressed at high levels in cervical cancer tissues and is negatively correlated with the level of infiltrating CD8⁺ T cells. In addition, In vitro and in vivo, reducing the expression of CD112 inhibited cell proliferation and migration. Antibody array-based profiling of protein analysis revealed that CD112 knockdown can inhibit the SLC7A11/GPX-4 pathway and activate ferroptosis; the opposite effects were observed upon CD155 has overexpression. We further confirmed the mechanism between CD112 and SLC7A11/GPX-4 pathway through rescue experiments. CD112 overexpression reversed the ferroptosis effects and inhibition of the SLC7A11/GPX-4 pathway induced by GPX-4 inhibitor (rsl3).

Conclusion/Implications Our research demonstrated that CD112 can activate the SLC7A11/GPX-4 pathway and inhibit ferroptosis. Thus, CD112 is a potential screening and therapeutic biomarker for cervical cancer.

EP050/#898

DOES HIGHER NODAL DOSE IMPACT NODAL CONTROL IN CERVICAL CANCER: AN ANALYSIS OF PATIENTS TREATED WITH NODAL SIMULTANEOUS INTEGRATED BOOST FOR CERVICAL CANCER

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Introduction The dose prescription for nodes is heterogeneous and choice of optimal dose is unclear. This study was designed to report nodal response in patients receiving simultaneous integrated boost (SIB) for stage IIIC cervical cancer.

Methods Patients who received chemoradiation and nodal dose escalation through SIB followed by brachytherapy were included. As per RECIST 1.1, baseline lymph node was categorized as pathological if short axis diameter (SAD) was ≥ 10 mm and measurable if SAD ≥ 15 mm or as a non-target if SAD ≥ 10 mm, but < 15 mm. On follow-up, if SAD was < 10 mm, the node was considered non-pathologic. Nodal Control and Disease-Free Survival (DFS) was determined. Log-rank test was used for evaluation of impact of nodal RECIST baseline nodal category, nodal volume and dose on nodal control and disease-free survival (DFS).

Results Sixty-six patients with 153 nodes were included. Patient characteristics and treatment details are depicted in table 1. Median SIB dose was 55Gy (45-56.5Gy). Number of nodes receiving dose < 50 Gy were 7 (4.6%), 51-55Gy: 36 (23.5%) and > 55 Gy: 110 (71.9%). At response assessment 92.2% nodes (n=141) had complete response, 6.5% (n=10) had partial response and 1.3% (n=2) had progressive disease. The median follow up was 33 months (9-66 months). Patients receiving > 55 Gy had better 5-year nodal control (84.6% vs 58.7% p=0.02, figure 1). Reduced 5-yr DFS (76% vs 44%, p=0.15) was also observed based on RECIST definition though it was not statistically significant.